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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/765,694	01/27/2004	Sherwin V. Kevy	1459.008A	1436

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EXAMINER	
SCHUBERG, LAURA J	

ART UNIT	PAPER NUMBER
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/765,694	KEVY ET AL.	
	Examiner	Art Unit	
	Laura Schuberg	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *19 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☒ Claim(s) *3* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-20 are pending.

Claims 19 and 20 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/16/2006.

Claims 1-18 have been examined on the merits.

Response to Arguments

Applicant's arguments with respect to claims 1-18 have been considered but are moot in view of the new ground(s) of rejection.

Claim Objections

Claim 3 is objected to because of the following informalities: The anticoagulants should all be spelled out initially next to the shortened terminology for clarity purposes. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent

granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, 4, 12-16 rejected under 35 U.S.C. 102(b) as being anticipated by Xiao et al. (Scand J Clin Lab 1998).

Claim 1 is drawn to a method for the production of a coagulant from anticoagulated whole blood comprising:

a) obtaining a volume of anticoagulated whole blood from a subject;

b) mixing the anticoagulated whole blood with a precipitating agent;

c) incubating the mixture of b) for a time sufficient to produce cellular and specific plasma component precipitate and a supernatant;

d) separating the precipitate from the supernatant;

e) recovering the supernatant wherein the supernatant is used as a coagulant.

Claim 3 is drawn to wherein the whole blood is anticoagulated with an anticoagulant selected from the group consisting of ACD, ACD/mannitol, CPD, and EDTA.

Claim 4 is drawn to wherein the whole blood is anticoagulated with ACD.

Claims 12 and 13 include wherein the incubation step requires less than 45 minutes and 30 minutes respectively.

Claim 14 includes wherein the coagulant prepared is autologous.

Claim 15 includes wherein the coagulant prepared is homologous.

Claim 16 includes wherein the separating step is centrifuging the mixture.

Xiao et al. teaches a method wherein whole blood is treated with an anticoagulant (EDTA), mixed with a precipitating agent for about 20 seconds, centrifuged for 10 minutes and the supernatant is collected (page 506, column 2 lines 4-23). Other anticoagulants are used as well such as ACD (page 507 column 2 lines 1-13). While the reference supernatant is not used as a coagulant in the referenced method, the phrase " recovering the supernatant wherein said supernatant is used as a coagulant" is deemed to be an intended use for the coagulant in the claimed production method and as such would not appear to define the claimed supernatant over the prior art. In addition, wherein the coagulant prepared is autologous or homologous are also deemed to be intended use limitations of the claimed supernatant since they depend upon how the supernatant is used after production.

Therefore, the method of Xiao et al. anticipates Applicant's invention as claimed.

Claims 1, 7, 8, 11, 14, 15, 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Coelho et al. (US 6,472,162).

Claim 7 includes wherein the precipitating agent is ethanol.

Claim 8 includes wherein the ethanol used is at a starting concentration of about 10% to 100%.

Claim 11 includes wherein the precipitating agent is a mixture of ethanol and calcium chloride.

Claim 17 includes wherein the separating step is by filtering the mixture.

Coelho et al. teach a method for extracting and then dispensing thrombin consisting of taking whole blood from a person, sequestering prothrombin from the whole blood by addition of ethanol (mixing, incubating, and collecting), wherein ethanol is present at a concentration between 8% and about 20% and converting prothrombin to thrombin (column 12 claim 17). Filtering is used to separate the precipitate from the supernatant and calcium chloride is added with the ethanol (column 10 lines 7-49). Wherein the coagulant prepared is autologous is specifically taught (column 6 line 46) as well as sourced from a single donor (homologous) (column 6 line 11).

Coelho et al. is silent to the use of an anticoagulant in the whole blood, however the use of whole blood after it is drawn inherently requires the use of an anticoagulant to prevent the blood from being rendered useless by the natural clotting process. Therefore, the use of whole blood that has been exposed to an anticoagulant is deemed to be an inherent condition of the reference method.

Therefore, the method of Coelho et al. inherently anticipates Applicant's invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 2, 3, 7-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gray et al. (US 4,680,177) in view of Cochrum et al. (US 5,773,033).

Claim 2 includes wherein the volume of anticoagulated whole blood is between 8 to 10 ml.

Claims 8-10 include wherein the ethanol used is at a starting concentration of about 10% to 100%, about 25% to 95%, about 50% to 95% respectively.

Gray et al. teach a method for the production of blood products wherein anticoagulated whole blood or blood plasma is processed by cryoprecipitation to yield a precipitate that is separated from the supernatant (column 4 lines 39-49). While blood plasma is indicated as preferred over whole blood (column 4 lines 9-21), whole blood is clearly indicated as an option (column 4 line 39 and column 8 lines 45-58). Anticoagulation with neutral salts is indicated as preferred when coagulant activity in the precipitate is desired(column 4 lines 39-50), the use of anticoagulants such as CPD, ACD or EDTA are indicated as less preferred options since they leave more coagulant

activity in the remaining supernatant (column 4 line 1-57), and are used for comparisons (column 8 lines 45-58). Blood is taken from a mammalian donor (homologous) (column 3 lines 55-60). Calcium chloride is taught as a possible option as an anticoagulant (column 6 lines 37-40).

Gray et al. do not teach the mixing of the anticoagulated whole blood with a precipitating agent, wherein the volume of anticoagulated whole blood is between 8 to 10 ml, or wherein the coagulant is autologous.

Cochrum et al. teach that suitable methods of precipitation of blood include cryoprecipitation or precipitation by using ethanol (column 2 lines 15-25). Cochrum et al. also teach that it is preferable when producing blood products to use the patient's own blood (column 2 lines 41-55).

Therefore, one of ordinary skill in the art would have been motivated to substitute different methods of precipitation (such as ethanol precipitation) for cryoprecipitation in the method of Gray et al. with a reasonable expectation of success because Cochrum et al. teaches that these are art recognized equivalents for forming precipitates from blood.

The amount of whole blood and ethanol used and the length of time for incubation would have been a matter of routine optimization depending on the final amount of coagulant or blood component needed. One of ordinary skill in the art would have been motivated to use the smallest amount of blood possible when drawing from the same patient to minimize blood loss during surgery. One of ordinary skill in the art

would have used the shortest incubation time in order to supply the coagulant or blood component to the patient as quickly as possible.

One of ordinary skill in the art would have been motivated to use autologous blood in the method of Gray et al. with a reasonable expectation of success because Cochrum et al. teaches that autologous blood is preferable to reduce disease transmission (column 2 lines 50-55).

Therefore, the combined teachings of Gray et al. and Cochrum et al. render obvious Applicant's invention as claimed.

Claims 1-4, 7-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coelho et al. (US 6,472,162) in view of Rock (US 4,359,463).

Claim 18 includes wherein the separating step is a combination of centrifugation and filtration of the mixture.

Coelho et al. teach a method for extracting and then dispensing thrombin consisting of taking whole blood from a person, sequestering prothrombin from the whole blood by addition of ethanol (mixing, incubating, and collecting), wherein ethanol is present at a concentration between 8% and about 20% and converting prothrombin to thrombin (column 12 claim 17). Filtering is used to separate the precipitate from the supernatant and calcium chloride is added with the ethanol (column 10 lines 7-49) however both filtering and centrifugation are taught as suitable methods for separating precipitate from supernatant (column 9 lines 13-17). Wherein the coagulant prepared is

autologous is specifically taught (column 6 line 46) as well as sourced from a single donor (homologous) (column 6 line 11). While Coelho et al. are silent with regard to the amount of whole blood required; the apparatus used for the method is capable of receiving a volume of 15 ml (column 9 line 42). The incubation time is taught at about 60 minutes or 30 to 75 (column 10 lines 27 and 42).

Rock teaches a method of treating whole blood to obtain Factor VIII and that whole blood that is withdrawn from a patient is generally collected with an anticoagulant (column 1 lines 14-17). Commonly used anticoagulants include ACD, CPD and EDTA (column 2 line 63 – column 3 line 6).

While the addition of an anticoagulant is considered to be inherent to the method of Coelho et al. as described above, even if it had not been inherent, it would have been obvious for one of ordinary skill in the art to add the anticoagulant to the whole blood in the method of Coelho et al. The artisan of ordinary skill would have been motivated with a reasonable expectation of success by the fact that it was common practice to add anticoagulants to blood collected for the purpose of obtaining blood products as taught by Rock.

Coelho et al. does not teach the amount of whole blood to be used, higher concentration levels of ethanol, or incubation times of less than 30 minutes. However these variables would have been a matter of routine optimization depending on the final amount of coagulant needed. One of ordinary skill in the art would have been motivated to use the smallest amount of blood possible when drawing from the same patient to minimize blood loss during surgery. One of ordinary skill in the art would have used the

shortest incubation time in order to supply the coagulant or blood component to the patient as quickly as possible. One of ordinary skill in the art would have optimized the concentration of the ethanol to obtain a product of the highest amount with the highest purity in the shortest amount of time possible. One of ordinary skill in the art would have been motivated to use both centrifugation and filtering to separate the precipitate from the supernatant in order to improve the quality and purity of the final product. One of ordinary skill in the art would have had a reasonable expectation of success because Coelho et al. do suggest that modifications and adaptations of the method may be applied to the method as needed (column 11 lines 34-39).

Therefore, the combined teachings of Coelho et al. and Rock render obvious Applicant's invention as claimed.

Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coelho et al. (US 6,472,162) in view of Rock (US 4,359,463) as applied to claims 1-4, 7-18 above, and further in view of Sato et al (US 4,812,310).

Claim 5 includes wherein the anticoagulant is ACD/mannitol.

Claim 6 includes wherein the mannitol is present in a concentration of 7.5 mg/ml ACD.

The combination of Coelho et al. and Rock teach the invention of claims 1-4 and 7-18 as described above, but do not specifically mention that mannitol is to be used in combination with ACD.

Sato et al. teaches that by adding mannitol to blood, the swelling of blood cells can be prevented during the preservation (column 4 lines 32-34). Sato et al. teach that it has been found that by adding mannitol to a conventional preserving solution such as ACD that the concentration depends on the amount of blood to be preserved, the decrease in Na+ concentration and the increase in K+ concentration in the plasma for the hemolysis to be prevented (column 4 lines 40-50). Sato et al. teach that mannitol was usually added in an amount of 0.67 to 6.7 w/v% (column 5 line 66).

One of ordinary skill in the art would have been motivated to add mannitol to the ACD anticoagulant in the method of Coelho et al because Sato et al. teaches that by adding mannitol to blood, the swelling of blood cells can be prevented during the preservation (column 4 lines 32-34). One of ordinary skill in the art would have had a reasonable expectation of success because Coelho et al. do suggest that modifications and adaptations of the method may be applied as needed (column 11 lines 34-39) and Sato et al. teach that this modification is applicable to the preservation of a blood preparation, particularly whole blood (column 6 lines 30-35).

The concentration of mannitol used with ACD in the method of Coelho et al. would have been a matter of routine optimization. One of ordinary skill in the art would have been motivated to adjust the level of mannitol since Sato et al. teach that the concentration depends on the amount of blood to be preserved, the decrease in Na+ concentration and the increase in K+ concentration in the plasma (column 4 lines 40-50). One of ordinary skill in the art would have had a reasonable expectation of success because Sato et al. teach a range of concentrations for optimization (column 5 line 66).

Therefore, the combined teachings of Coelho et al., Rock and Sato et al. render obvious Applicant's invention as claimed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3 and 4 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-18 and 20 of copending Application No. 11/200,535. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the co-pending application include all the limitations of the instant application and therefore anticipate the claims of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura Schuberg whose telephone number is 571-272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Laura Schuberg